

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 August 2001 (30.08.2001)

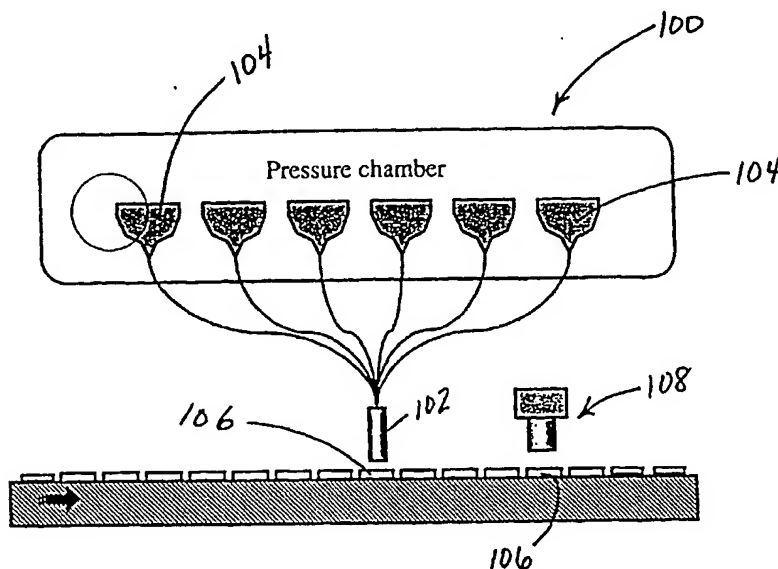
PCT

(10) International Publication Number
WO 01/62378 A3

- (51) International Patent Classification⁷: **B01J 19/00**, **B01L 3/00**
- (21) International Application Number: **PCT/US01/05844**
- (22) International Filing Date: **22 February 2001 (22.02.2001)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:
60/183,737 22 February 2000 (22.02.2000) US
60/188,872 13 March 2000 (13.03.2000) US
60/216,265 6 July 2000 (06.07.2000) US
60/220,085 21 July 2000 (21.07.2000) US
60/244,413 30 October 2000 (30.10.2000) US
- (72) Inventors; and
(75) Inventors/Applicants (for US only): **CHEN, Shing** [GB/US]; 13818 Goosefoot Terrace, Rockville, MD 20850 (US). **LUO, Yuling** [US/US]; 46540 Fremont Boulevard, Suite 506, Fremont, CA 94538 (US). **CHEN, Anthony, C.** [US/US]; 46540 Fremont Boulevard, Suite 506, Fremont, CA 94538 (US).
- (74) Agents: **HOLLAND, Charles, D.** et al.: Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, CA 94304-1018 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (71) Applicant (for all designated States except US): **GENOSPECTRA, INC.** [US/US]; 46540 Fremont Boulevard, Suite 506, Fremont, CA 94538 (US).
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian

[Continued on next page]

(54) Title: **MICROARRAY FABRICATION TECHNIQUES AND APPARATUS**



Schematic configuration of invented microarray fabrication system

(57) Abstract: Disclosed is a microarray printing system and methods of printing probe microarrays 1000. The system has a print-head (102, 606, 706, 806) formed of one or more capillary bundle (104), such as light-guiding capillaries. The bundles (104) may especially be bundles (104) of capillaries that provide a large number of probes 1004 on the surface of a substrate. Methods of registering or correlating the distal 112 and proximal 110 ends of the capillaries are also provided. Further, the invention provides methods and equipment for identifying defective microarrays 1000 that are missing one or more probes from the surface of the microarray 1000.



patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(88) Date of publication of the international search report:
7 February 2002

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 01/05844

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01J19/00 B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01L B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, INSPEC, COMPENDEX, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MARK SCHENA ET AL.: "Microarrays: biotechnology's discovery platform for functional genomics" TIBTECH, vol. 16, no. 7, 1 July 1998 (1998-07-01), pages 301-306, XP004145643 CAMBRIDGE, UK ISSN: 0167-7799 the whole document	52-63
X	MICHAEL B. EISEN ET AL.: "12 DNA ARRAYS FOR ANALYSIS OF GENE EXPRESSION" METHODS IN ENZYMOLOGY, vol. 303, 1999, pages 179-205, XP000995864 SAN DIEGO, CA, USA ISSN: 0076-6879 page 188, paragraph 2 -page 189, paragraph 1	52-63

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

19 October 2001

Date of mailing of the international search report

26/10/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Stevnsborg, N

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/05844

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BERTRAND LEMIEUX ET AL. : "OVERVIEW OF DNA CHIP TECHNOLOGY"</p> <p>MOLECULAR BREEDING: NEW STRATEGIES IN PLANT IMPROVEMENT ,</p> <p>vol. 4, 1998, pages 277-289, XP000915221</p> <p>NL</p> <p>ISSN: 1380-3743</p> <p>page 277, right-hand column, last paragraph -page.278, left-hand column, paragraph 1</p> <p>page 281, right-hand column, paragraph 3</p> <p>---</p>	52-63
X	<p>MARK SCHENA : "GENOME ANALYSIS WITH GENE EXPRESSION MICROARRAYS"</p> <p>BIOESSAYS,</p> <p>vol. 18, no. 5, 1996, pages 427-431, XP002916033</p> <p>CAMBRIDGE, UK</p> <p>ISSN: 0265-9247</p> <p>page 427, right-hand column, last paragraph -page 428, left-hand column, paragraph 2</p> <p>---</p>	52-63
X	<p>DEVAL A. LASHKARI ET AL. : "Yeast mmicroarrays for genome wide parallel genetic and gene expression analysis"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE,</p> <p>vol. 94, November 1997 (1997-11), pages 13057-13062, XP002115013</p> <p>WASHINGTON, DC, USA</p> <p>ISSN: 0027-8424</p> <p>abstract; figure 1</p> <p>---</p>	52-63
X	<p>YU-HUI ROGERS ET AL.: "IMMOBILIZATION OF OLIGONUCLEOTIDES ONTO A GLASS SUPPORT VIA DISULFIDE BONDS: A METHOD FOR PREPARATION OF DNA MICROARRAYS"</p> <p>ANALYTICAL BIOCHEMISTRY,</p> <p>vol. 266, no. 1,</p> <p>1 January 1999 (1999-01-01), pages 23-30, XP001005968</p> <p>SAN DIEGO, CA, USA</p> <p>ISSN: 0003-2697</p> <p>abstract</p> <p>page 25, left-hand column, paragraph 3 - paragraph 4</p> <p>page 27, left-hand column, paragraph 2</p> <p>-page 28, right-hand column, paragraph 1</p> <p>---</p> <p>-/--</p>	52-63

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/05844

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 01798 A (CARTESIAN TECHNOLOGIES) 13 January 2000 (2000-01-13) page 1, line 21 - line 23 page 9, line 14 - line 19 page 15, line 33 -page 16, line 4 ---	52-63
X	US 5 807 522 A (PATRICK O. BROWN & TIDHAR DARI SHALON) 15 September 1998 (1998-09-15) cited in the application column 4, line 16 - line 23 column 6, line 32 - line 38 column 9, line 30 - line 45 column 15, line 19 - line 43 ---	52-63
X	WO 98 55593 A (MOLECULAR TOOL, INC.) 10 December 1998 (1998-12-10) page 14, line 11 - line 31 ---	52-63
X	WO 99 40434 A (INVITROGEN) 12 August 1999 (1999-08-12) page 15, paragraph 2 ---	52-63
X	US 5 690 894 A (DANIEL PINKEL & JOE GRAY) 25 November 1997 (1997-11-25) column 3, line 1 - line 30 column 7, line 1 -column 9, line 55 figures ---	52-63
X	WO 00 01859 A (ORCHID BIOCOMPUTER, INC.) 13 January 2000 (2000-01-13) cited in the application the whole document ---	1-5,13, 19,24, 37-39, 42,43, 52-63
A	WO 99 55461 A (CORNING INCORPORATED) 4 November 1999 (1999-11-04) cited in the application the whole document ---	1-28,38
X	WO 98 29736 A (GENOMETRIX INCORPORATED) 9 July 1998 (1998-07-09) cited in the application page 22, line 11 -page 24, line 17 page 27, line 6 -page 28, line 15 page 42, line 20 -page 43, line 8 figures 4,4A,4B --- -/--	1-5,8,9, 13,15, 19,21, 22,24, 25,28, 37,38, 52-63

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/05844

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 630 925 A (STEPHEN L. PENTONEY, JR. & KENNETH D. KONRAD) 20 May 1997 (1997-05-20) ---	
X	WO 99 13312 A (MOLECULAR DYNAMICS, INC.) 18 March 1999 (1999-03-18) page 1, line 12 - line 36 page 12, line 14 - line 18 page 15, line 16 - line 34 page 20, line 30 -page 21, line 37 page 24, line 15 -page 26, line 31 figures 6,11,11A,14 ---	1-5,7-9, 13,19, 21,22, 24,25, 27,28,31
X	PATENT ABSTRACTS OF JAPAN vol. 1995, no. 04, 31 May 1995 (1995-05-31) -& JP 07 023995 A (YOSHIHIRO KISHIGAMI), 27 January 1995 (1995-01-27) abstract -----	1-5

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box 1.2

Claims Nos.: 29-37, 39-63; 1-28, 38 (in part)

In view of the large number and also the wording of the claims presently on file, it is difficult, if not impossible, to determine the exact subject matter for which protection is sought.

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty for the subject matter of microarrays. So many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible.

Moreover, present claims 1-63 relate to an extremely large number of possible capillary bundles, print heads comprising a capillary bundle for printing microarrays, print systems comprising the print heads, methods of forming capillary bundles, methods of making or printing arrays, and microarrays. In fact, the claims contain so many options, variables, and possible permutations that a lack of clarity and/or conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

The present therefore application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear and concise, namely

I: A print system and a method for forming microarrays, which system comprises a print head formed from a bundle of capillaries, the capillaries being in fluid communication at their distal ends with a plurality of reservoirs, and their proximal ends being adapted for depositing fluids on a support surface, wherein the proximal and distal ends of the capillaries are coated with electrically conductive material, and which system also comprises a voltage source for moving fluid through the capillaries.

II: The method comprises passing fluid through the capillaries by means of a voltage potential between the distal and the proximal ends thereof, thereby depositing fluids in an array on a solid support surface.

Consequently, the search has been restricted to those parts of claims 1-28 and 38 which relate to the subject matter referred to in (I) and (II) above.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/05844

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0001798	A	13-01-2000	AU 4861099 A CN 1315913 T EP 1129008 A2 WO 0001798 A2	24-01-2000 03-10-2001 05-09-2001 13-01-2000
US 5807522	A	15-09-1998	AT 180570 T AU 709276 B2 AU 2862995 A CA 2192095 A1 DE 69509925 D1 DE 69509925 T2 DK 804731 T3 EP 0804731 A1 EP 0913485 A1 ES 2134481 T3 GR 3030430 T3 JP 10503841 T US 6110426 A WO 9535505 A1	15-06-1999 26-08-1999 15-01-1996 28-12-1995 01-07-1999 09-12-1999 08-11-1999 05-11-1997 06-05-1999 01-10-1999 30-09-1999 07-04-1998 29-08-2000 28-12-1995
WO 9855593	A	10-12-1998	US 5919626 A AU 7726098 A EP 0996705 A1 WO 9855593 A1 US 6136962 A	06-07-1999 21-12-1998 03-05-2000 10-12-1998 24-10-2000
WO 9940434	A	12-08-1999	AU 2583899 A EP 1060395 A1 WO 9940434 A1	23-08-1999 20-12-2000 12-08-1999
US 5690894	A	25-11-1997	US 6146593 A	14-11-2000
WO 0001859	A	13-01-2000	US 6235473 B1 AU 4855999 A WO 0001859 A2	22-05-2001 24-01-2000 13-01-2000
WO 9955461	A	04-11-1999	EP 0955084 A1 AU 3552499 A AU 3760499 A CN 1311717 T EP 1075327 A1 WO 9955460 A1 WO 9955461 A1	10-11-1999 16-11-1999 16-11-1999 05-09-2001 14-02-2001 04-11-1999 04-11-1999
WO 9829736	A	09-07-1998	AU 6646398 A EP 0990142 A1 JP 2001510339 T US 6083763 A WO 9829736 A1	31-07-1998 05-04-2000 31-07-2001 04-07-2000 09-07-1998
US 5630925	A	20-05-1997	AU 6543696 A EP 0838029 A1 JP 11509625 T WO 9703352 A1	10-02-1997 29-04-1998 24-08-1999 30-01-1997
WO 9913312	A	18-03-1999	US 6190616 B1 EP 1019694 A1 WO 9913312 A1	20-02-2001 19-07-2000 18-03-1999

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/05844

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9913312 A		US 2001007641 A1	12-07-2001
JP 07023995 A	27-01-1995	JP 8017785 B	28-02-1996